REMARKS

Claims 1 and 2 have been amended as noted above. Support for these amendments may be found in the specification at, for example, page 4, lines 9-21; page 5, lines 31-35; page 6, lines 1 to 29; and Examples 1-4.

Claims 6, 13, and 16 have been amended to recite "1 to 120 hours" rather than "1 to 120 h." This amendment is for clarification only and does not change the scope of the claims.

Claim 8 has been amended to recite "with an enzyme obtained from *G. oxydans* DSM 4025, (b) converting the substrate into L-ascorbic acid by catalytic activity of the enzyme in a microorganism capable of such conversion at a pH of about 1 to about 9 and at a temperature of about 13°C to about 45°C..." Support for this amendment may be found in the specification at, for example, page 1, lines 18-21; page 5, lines 31-35; page 6, lines 1 to 29; and Examples 1-4.

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments is respectfully solicited.

Claim Objections

Claims 1 and 2 were objected to because they recite the phrase "...the complementary sequence thereof," and it was not clear to the Examiner "whether the complementary polynucleotide claimed is full length or partial complement of the claimed sequence." (Paper No. 20090501 at 2-3). In accordance with Examiner's suggestion and as noted above, claims 1 and 2 are amended to recite "the full-length

complement of the DNA sequence of SEQ ID NO:1." Accordingly, it is respectfully submitted that the objection has been rendered moot and should be withdrawn.

Rejections under 35 USC § 112 and 35 USC § 101

Claims 1 and 2, and claims 6, 7, and 13 depending therefrom were rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. (Paper No. 20090501 at 3). In making the rejection, the Examiner asserted that because claims 1 and 2 recite "under suitable culturing conditions" but "does not set forth any steps involved in the method i.e., either a host cell or a transformed host cell expressing the polypeptide of SEQ ID NO: 2, it is unclear what method applicant is intending to encompass." (*Id.*) The Examiner concluded that "[a] claim is indefinite where it merely recites a method without any active, positive steps delimiting how this method is actually practiced." (*Id.*)

The same claims were rejected under 35 USC § 101. (*Id.*) In making the rejection, the Examiner asserted that "the claimed recitation of 'a suitable culturing conditions[']', without setting forth any steps involved in the process i.e., host cell or transformed host cell, results in an improper definition of a process." (*Id.*)

Initially, we note that claims 1 and 2 are amended to recite "...converting the substrate into L-ascorbic acid by catalytic activity of the enzyme in a microorganism capable of such conversion at a pH of about 1 to about 9 and at a temperature of about 13°C to about 45°C..." It is respectfully submitted that as amended, claims 1 and 2 render the rejections moot, because the host organism is recited, and because the

specific conditions of reaction are recited. Hence, the steps involved in the method are set forth in the amended claims. According, the rejection should be withdrawn.

Rejection under 35 USC § 112 – Indefiniteness Rejection

Claims 8 and 16 were rejected under 35 USC §112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." (Paper No. 20090501 at 4).

In making the rejection, the Examiner asserted that "it is unclear what the phrase 'derivable from [G. *oxydans* DSM 4025]...' means" in the context of claims 8 and 16. (*Id.*). The Examiner questioned, "is this synonymous with 'obtained from specific strain or source' or does it include natural and man-made mutants thereof from any source." (*Id.*) The Examiner further asserts that "unless applicant has defined the term 'derivable ... ' as equivalent to 'obtained from the specific source with specific structure', the term 'derivable ...' does not further limit the recited enzyme." (*Id.*, emphasis original.)

In accordance with the Examiner's suggestion, claim 8 has been amended to recite "...obtained from G. *oxydans* DSM 4025." Accordingly, it is respectfully submitted that the rejection has been rendered moot and should be withdrawn.

Written Description/New Matter Rejection

Claims 1, 2, and 8, and claims 6, 7, 13, and 16 depending therefrom were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. (Paper No. 20090501 at 5).

In making the rejection, the Examiner asserted that "[c]laims 1, 2, 8 are rejected because the phrase 'directly' is new matter." (*Id.*) The Examiner also asserted that "[t]he scope of the process for the production of L-ascorbic acid comprising: (a) contacting an enzyme with a substrate which is selected from the group consisting of L-gulose, L-galactose, L-iodose and L-talose; (b) converting the substrate 'directly' into L-ascorbic acid .... as claimed was not contemplated in the specification as originally filed." (*Id.*, emphasis original)

The Examiner also asserted that "[the] claimed recitation of a use of Enzyme B ... (in page 1, lines 1-2 of specification), without setting forth any steps involved in the process, results in an improper definition of a process" and that "[t]he recitation of [the] phrase "use" without any active, positive steps delimiting how this use is actually practiced, renders the term indefinite and failing [sic] to particularly point out and distinctly claim the subject matter which applicant regards as the invention" (*Id.* at 7, emphasis original.)

Initially, we note that claims 1, 2 and 8 are amended to recite "...converting the substrate into L-ascorbic acid by catalytic activity of the enzyme in a microorganism capable of such conversion at a pH of about 1 to about 9 and at a temperature of about 13°C to about 45°C..." Accordingly, the rejection with respect to the phrase "directly" has been rendered moot and should be withdrawn.

We also note that the Examiner's assertion regarding the "improper definition of a process" refers to **not to any claim** of the application, but to **the first page of the specification**. 35 U.S.C. § 112 states, "[t]he specification shall conclude with one or more **claims** particularly pointing out and distinctly **claiming** the subject

matter which the applicant regards as his invention." This requirement is clearly directed towards **claims**. There is no requirement that other portions of the specification should distinctly claim the subject matter. Therefore, it is respectfully submitted that the rejection related to the "improper definition of a process" is inapplicable.

Accordingly, it is respectfully submitted that the written description rejection should be withdrawn.

Enablement Rejection

A. Direct Conversion.

Claims 1-2, 6-8, 13, and 16 were rejected under 35 USC §112, first paragraph, on the asserted grounds that the specification is not enabling. (Paper No. 20090501 at 8).

In making the rejection, the Examiner acknowledged that

> the specification ... [is] enabling for the production of L-ascorbic acid comprising: contacting an enzyme having the amino acid sequence of SEQ ID NO: 2 encoded by a polynucleotide of SEQ ID NO: 1, said polypeptide expressed in a specific strain of *E. coli* JM 109 having the activity to produce L-ascorbic acid from substrates L-gulono-1,4-lactone/L-gulonic acid from L-gulose and from L-galactono-1,4-lactone/L-galctonic [sic] acid or conversion of substrate L-galactose to L-galactono-1,4-lactone/L-galactonic acid and L-ascorbic acid under suitable culture conditions... (*Id.* at 8-9, emphasis original)

However, the Examiner asserted that

> the specification does not reasonably provide enablement for a process for the production of L-ascorbic acid comprising: contacting an enzyme with a substrate selected from the group consisting of L-gulose, L-galactose, L-idose, L-talose, L-gulono-1,4-lactone, L-gulonic acid, L-galactono-1,4-lactone, L-galactonic acid, L-idono-1,4-lactone, L-idonic

> acid, L-talono-1,4-lactone and L-talonic acid and converting the substrate directly into L-ascorbic acid by catalytic activity of the polypeptide comprising the amino acid sequence of SEQ ID NO: 2, encoded by the polynucleiotide of SEQ ID NO: 1 under undefined [sic] stringent hybridization and wash conditions and under specific defined process conditions such as pH, temperature and time in which said substrates are allowed to react with said enzyme. (*Id.* at 9, emphasis original.)

The Examiner asserted that "[t]he said process of production of L-ascorbic acid was carried out under specific cellular context ***in vivo***, ... and therefore said bacteria may provide other necessary enzymes either for the production of intermediate products of L-ascorbic with claimed substrates or for the final conversion of the intermediate products to L-ascorbic acid." (*Id.* at 10, emphasis original.) The Examiner concluded, "[t]herefore said process of production of L-ascorbic acid does not involve converting substrates directly into L-ascorbic acid and examiner is unable to find any support for claims as written." (*Id.*, emphasis added)

Although not explicitly set forth in the statute, enablement may be found where some experimentation (even a considerable amount) is required, so long as the experimentation is not "undue." *Ex parte Forman*, 230 USPQ 546, 547 (BPAI 1986); *see also In re Colianni*, 561 F.2d 220, 224, 195 USPQ 150, 153 (J. Miller concurring) (CCPA 1977); and *In re Rainer*, 347 F.2d 574, 577, 146 USPQ 218, 220-221 (CCPA 1965). The Federal Circuit, adopting the analysis set forth in *Forman*, has enumerated several factors which may be considered in determining whether claims require that one skilled in the art perform undue experimentation in order to practice the claimed subject matter: breadth of the claims; predictability or unpredictability of the art; relative skill of those in the art; state of the prior art; nature of the invention; working examples; amount of guidance; and quantity of experimentation necessary. *Wands*, 858 F.2d at 737, 8

USPQ2d at 1404. These factors are merely illustrative, not mandatory; they provide a general framework for analysis. *Enzo Biochem v. Calgene Inc.*, 188 F.3d 1362, 1371, 52 USPQ2d 1129, 1136 (Fed. Cir. 1999); *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir.), *cert. denied*, 502 U.S. 856 (1991).

Initially, we note that claims 1, 2 and 8 are amended to recite "...converting the substrate into L-ascorbic acid by catalytic activity of the enzyme in a microorganism capable of such conversion at a pH of about 1 to about 9 and at a temperature of about 13°C to about 45°C..." Thus, as amended, the claims recite a process for the production of L-ascorbic acid that is carried out by the enzyme in a microorganism capable of such conversion.

It is respectfully submitted that the specification is enabling with respect to the amended claims 1, 2, 6-8, 13 and 16. The working examples clearly demonstrate that such a process may be used for the production of L-ascorbic acid. For example, in Example 1 (pages 8-9) of the instant application, *E. coli* JM109 carrying pTrcMalE-EnzB (which contains the DNA sequence encoding an exogenous enzyme having the sequence of SEQ ID NO: 2 under a lac promoter control in a vector) was cultivated with or without IPTG in the presence of L-gulose. The results of the experiment are reproduced below for the convenience of the Examiner.

TABLE 1

Strain	IPTG	HPLC	
		L-GuL + L-GuA (mM)	L-ascorbic acid (mg/L)
JM109/pTrcMalE-EnzB	+	8.4	42.5
	-	4.6	10.5
JM109	+	nd	nd
	-	nd	nd

L-GuL: L-gulono-1,4-lactone; L-GuA: L-gulonic acid; nd: not detected

Similarly, Example 2 shows that only in the presence of the exogenous enzyme can *E. coli* JM109 produce vitamin C in the presence of L-gulono-1,4-lactone. Furthermore, the enzyme is again the determining factor in the production of vitamin C from L-galactose or L-galactono-1,4-lactone. (Examples 3 and 4).

The working examples cited above clearly demonstrate that the exogenous enzyme is the **key factor** in the conversion as set forth above, because *E. coli* JM109 without a vector encoding the exogenous enzyme having the sequence as set forth in SEQ ID NO:2 was unable to produce vitamin C in the presence of the starting substrates as cited above. It is further noted that the *E. coli* JM109 is one preferred example of such a microorganism. Even if other factors are required from *E. coli* or other microorganisms, production of vitamin C from one of the substrates as recited in claims 1, 2 or 8 is made possible with this exogenous enzyme.

Furthermore, the specification provides guidance as how to construct a microorganism carrying the gene for the exogenous enzyme (or its functional equivalent). *See* page 6, lines 1-14. The specification also provides guidance as to culture media and culturing conditions (page 6, lines 15-21; and page 6, line 29 to page

7, line 2). In addition, The conditions at which the process is carried out is also disclosed (page 6, lines 22-28), and the recovery of the products after reaction is specified (page 8, lines 4-9).

Given the amount of guidance present in the specification and the demonstration of the process by working examples, it is respectfully submitted that the specification is enabling with respect to the amended claims 1-2, 6-8, 13 and 16. Accordingly, the enablement rejection has been rendered moot and should be withdrawn.

B. Deposit

Claims 8 and 16 also were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. (Paper No. 20090501 at 11.)

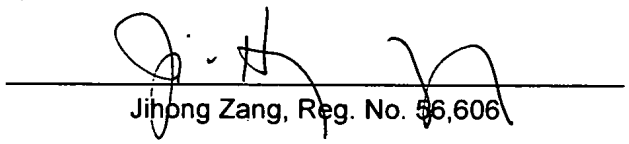
In making the rejection, the Examiner asserted that because "[i]t is apparent that a strain of G. *oxydans* DSM 4025 is required to practice the claimed invention," "the biological material must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public." (*Id.* at 12.) The Examiner asserted that "there is no indication in the specification as to the public availability." (*Id.*, emphasis original.) The Examiner further asserted that "[i]f a deposit was made under the terms of Budapest Treaty, then a statement, affidavit or declaration by Applicants, or a statement by an attorney of record over his/her signature and registration number, or someone empowered to make such a statement, stating that the invention will be irrevocably and without restriction released

to the public upon the issuance of a patent, would satisfy the deposit requirement made herein." (*Id.*)

Attached as Exhibit 1 hereto is a copy of a letter from the DSMZ depository, Deutsche Sammlung von Mikroorganismen und Zelkuturen GmbH, confirming that DSM 4025 (which was deposited at the DSMZ) is available to the public anywhere in the world without restrictions according to the rules of the Budapest Treaty from March 17, 1987 until March 17, 2032. Because DSM 4025 is already publicly available, the deposit requirement is already satisfied. Therefore, it is respectfully submitted that the rejection has been rendered moot and should be withdrawn.

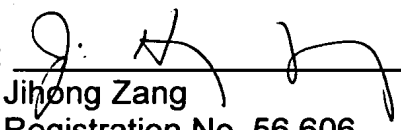
Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of the rejection, and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on November 10, 2008.



Jihong Zang, Reg. No. 56,606

Respectfully submitted,

By: 

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Ihr Zeichen / Your ref.	Unser Zeichen / Our ref.	Tel. 05 31 / 26 18 -	Datum/Date
Pa/dr	P 487 98/H	254	04.12.1998

CONFIRMATION

The following microorganism, deposited with the DSMZ - Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH under the Budapest Treaty, is freely available to the public anywhere in the world without restrictions according to the rules of the Budapest Treaty:

Gluconobacter oxydans - DSM 4025

as from March 17, 1987 until March 17, 2032.

The microorganism deposit in question is not listed in any publicly available catalogue of the DSMZ.

Yours faithfully,

DSMZ-Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH

U. Weihs

Dr. Vera Weihs

Geschäftsführer:
Prof. Dr. Erko Stackebrandt

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